BULLETIN

of the

ONTARIO COLLEGE OF PHARMACY

Vol. I, No. 5 H. J. Fuller, Editor November, 1952

CONTENTS.

		page
The "Foundation" for the Future	F. N. Hughes	cover
Isonicotinic Acid Hydrazide in Tuberculosis	G. C. Walker	28
Methyl Cellulose	H. A. Smythe	29
New Uses for the Enzyme Trypsin	R. M. Baxter	31
Nalline - A Narcotic Antagonist	G.R. Paterson	31
Registrar's Office	H.M. Corbett	32
Recent Research in Hypertension	R. M. Baxter	33
Cumulative Index		33

THE "FOUNDATION" FOR THE FUTURE

One Canadian pharmaceutical organization is most appropriately named because it is doing much to build solidly a foundation for a greater Pharmacy of the future. This body is, of course, the Canadian Foundation for the Advancement of Pharmacy.

The Foundation deserves the regular financial support of every pharmacist. Its current annual budget calls for $24,000 to be expended on scholarships, fellowships, extension courses, etc. Without its past help this and other colleges would have been unable to obtain sufficient qualified faculty personnel, fewer extension courses would have been offered, many students would have been unable to do post-graduate work.

With our natural pride in Ontario pharmacists it has been disappointing to learn, that the response from our group has been slow for the current fiscal year (June 1st, 1952 to May 31st, 1953). An annual amount of $5.00 is suggested from each pharmacist. We have over 2,200 pharmacies in Ontario, but only $1,600 has been received this year to date. Retail pharmacists in a neighbouring province have nearly doubled that. If you have not yet done so, we know you will wish to "help build the foundation".

Contributions should be sent to Mr. A. A. Brown, Executive Secretary-Treasurer, The Canadian Foundation for the Advancement of Pharmacy, 221 Victoria Street, Toronto.

F. N. Hughes.

We learn from the Registrar's Office that the ballots coming in show a 100 : 1 majority in favour of the proposal to enter into agreement with the University of Toronto for the establishment of a Faculty of Pharmacy.

Published five times a year, January, March, May September, November, by the authority of the Council of the Ontario College of Pharmacy, Editorial Office, 46 Gerrard Street East, Toronto, Ontario.

COMMITTEE ON EXTENSION SERVICES

H. J. Fuller, Chairman	Faculty
F. N. Hughes	Faculty
M. Haberman	District No. 5
W. S. Luton	District No. 8
C. P. Taylor	District No. 4

FACULTY.

R. O. Hurst, Phm. B. (Tor.) Dean Emeritus

F. Norman Hughes, Phm. B. (Tor.), B.S. in Phar. (Purdue), M.A. (Tor.)
Dean of Faculty, Professor of Materia Medica and Pharmaceutical Chemistry.
George C. Walker, B.Sc. (Pharm.) (Alta.), M.S., Ph.D. (Purdue),
Associate Professor of Pharmacy.
Horace J. Fuller, Phm. B. (Tor.), B.A. (West.), M.A. (Yale),
Associate Professor of Pharmacy in charge of Pharmacy Administration.
Daniel H. Murray, Phm.B. (Tor.), B.S.P., B.A., M.A. (Sask.),
Assistant Professor of Pharmaceutical Chemistry.
Ross M. Baxter, Phm.B. (Tor.), B.S.P. (Sask.), M.S., Ph.D. (Fla.)
Assistant Professor of Materia Medica.
G. R. Paterson, Phm.B. (Tor.), B.S.P., M.Sc. (Sask.),
Assistant Professor of Pharmaceutical Chemistry.
Allan M. Goodeve, Phm.B. (Tor.), B.S.P. (Sask.), Lecturer in Pharmacy.
Mrs. I. E. Stauffer, B.Sc., (Pharm.) (Alta.), M.Sc. (Western Reserve),
Special Lecturer in Hospital Pharmacy
Paul P. I. Sun, B.Sc. (Pharm.) (West China), Instructor in Pharmacy
D. Barton, Phm.B., B.Sc.Phm., (Tor.), Assistant in Pharmaceutical Chemistry
G. E. Brooks, B.Sc. Phm. (Tor.), Assistant in Pharmaceutical Chemistry
Miss D. L. Brygider, Phm.B. (Tor.), Assistant in Pharmacy
Miss S. M. Elliott, Phm.B. (Tor.), Assistant in Pharmacy
G. Murray Hetherington, Phm.B. (Tor.), Assistant in Pharmacy
Mrs. R. E. Smith, Phm.B. (Tor.), Assistant in Pharmacy

ADMINISTRATIVE STAFF

H. M. Corbett, Phm.B. (Tor.), Registrar-Treasurer
Miss F. M. Ward, B.A., Secretary to the Registrar
Miss H. M. Walton, Librarian
Miss Irene Hoy, Secretary
W. G. Smith, Inspector.

The recent advent of isonicotinic acid hydrazide (isoniazid) and its derivatives in the treatment of tuberculosis has created quite a good deal of interest particularly with the lay public. Research in this field was initiated as far back as the end of the last war and much progress was made both in Europe and in the U. S.A. Investigations by Hoffman-La Roche and E.R. Squibb resulted in the synthesis of isonicotinic acid derivatives with a pronounced activity against the tubercle bacillus both in the test tube and in animals. Clinical work in New York City found isonicontinic acid hydrazide to have a favourable effect in cases of advanced tuberculosis with only minor toxic effects and in addition, it was effective when administered orally in tablet form. Fever and cough were diminished, appetite and vitality were increased and a certain clearing of reversible lesions was observed.

The drugs have been tested in many hospitals and sanitaria and it is still not known whether they merely inhibit the growth of the tubercle bacillus or whether they can produce an actual cure. Development of resistance to the drugs has been noted in some cases and extended investigation is indicated to answer the question of resistance and other questions such as the length of administration, dosage forms, mechanisms of action, etc. It appears that more favourable effects can be secured by using para-amino salicylic acid and streptomycin in conjunction with the isonicotinic substances. The toxicity in man seems of little importance but several side-effects of a more or less transitory nature have been observed as for example, constipation, eosinophilia, exaggeration of reflexes. The daily dose is about 150 to 300 mg. administered in 2 or three fractional doses.

Specialty Products - Isonicotinic Acid Hydrazide and Related Products.

Product	Manufacturer	Product	Manufacturer
Aldinamide (pyrazinamide)	Lederle, U.S.A.	Nicetal	Wander, U.S.A.
Armazide	Armour, U.S.A.	Nicotibina	Le Petit (Italy)
Cotinazine	Pfizer, U.S.A.	Nitadon	Organon, Europe
Dinacrin	Winthrop, U.S.A.	Nydrazid	Squibb, U.S.A.
Ditubin	Schering, U.S.A.	Nysozid	NyscoLab., U.S.A.
Fimalene	U.C.B., Brussels	Pycazide	Hert Pharmaceuticals England
I N K	Lilly, U.S.A.	Pyricidin	Charles E. Frosst, Canada
Isolyn	Abbott, U.S.A.		
Isonizide (Iosonizide)	Panray, U.S.A.	Rimifon	Hoffman-La Roche, U.S.A. and Switzerland
Marsilid (the Isopropyl Derivative)	Roche, U.S.A. and Switzerland	Tibione (Amithiozone)	Schenley, U.S.A.
Mybasan	Antigen Lab. End.	Tizide	Pharmachemie, Pays-Bas
Neoteben	Bayer, Germany	Tubicon	Brocades, Pays-Bas
		Tubonel	Benger Lab., England
		Vederon	Carlo Erba, Italy

These new antitubercular drugs have been available in Canada for research in sanitaria, hospitals, etc. but the Department of National Health at Ottawa has now announced the release of the isonicotyl and isopropyl hydrazide compounds as of October 1, 1952, for sale on prescription only. The department emphasized the necessity for regarding the drugs as useful adjuncts to the armamentarium of antitubercular agents and not as cure-alls.

G. C. Walker

The past ten years has brought forward a host of new chemical compounds useful to the pharmacist, as physical aids to emulsions and other similar mixtures. Notable among these substances are the familiar spans, tweens, arlacels, and one lesser known - methyl cellulose. This chemical compound has the property of forming gels or sols with water which are quite stable, and which have a large potential for use in pharmaceutical mixtures.

CHEMISTRY

Methyl cellulose is white, odourless, tasteless, water-dispersible cellulose ether, prepared by treating cellulose with sodium hydroxide and then chloroform, as illustrated in the following simplified equation:

Where ROH is a single cellulosic hydroxyl:

$$ROH + CH_3Cl \xrightarrow{NaOH} NaCl + H_2O + ROCH_3 \quad \text{(Methyl Cellulose)}$$

PROPERTIES.

Methyl cellulose is soluble (i.e. will form gels and sols) in cold water, but not in hot water. It is stable in alkaline and dilute acidic solution (over a pH range of 2-12). The sols and gels formed with water are stable to heat and cold. Methyl cellulose is insoluble in most organic solvents, and in concentrated solutions of salts. It is combustible, but no more so than ordinary absorbent cotton. It is not affected by oils. When placed in solution it tends to foam, but this may be prevented by the use of any one of a number of commercially available antifoam compounds.

Methyl cellulose is available commerically in a wide range of viscosity types, ranging through 15-25-400-1500-4000 centipoises (a physical measure of viscosity). It is also available in a number of special types, such as :

* Methocel HG - High gel temperature
  Methocel AS - Soluble in 4% or stronger caustic solutions, but not in water alone
  Methocel CAM - Crude - containing 25-30% active ingredient, but having no fixed gel point.
* Methocel is the registered trade mark of the Dow Chemical Co.

USES

The foregoing properties of methyl cellulose have adapted it for use in many industries. It is used as a binder in pencil leads, and as an adhesive in starch pastes. The agricultural industry employs it as a binding agent for seed coating. It is used in the ceramics industry as a temporary binder in forming refractory bricks and shapes. It finds use also in the manufacture of synthetic rubber, and in the pasting of leather. It is an ingredient in water-soluble paints to prevent the settling out of the pigment. It is also used in "scrub-off" types of paint removers. Because of its purity (it contains no foreign substances) it does not encourage the growth of micro-organisms and may be used in foods which are to be stored for protracted periods. Its stability in acid media permits its use in such foods as salad dressing.

The pharmaceutical uses are even more extensive. Of course, one use of methyl cellulose (and chemically related substances), familiar to all, is as a bulk-producing laxative. This use is possibly due to the property of absorbing water from the tissues to form a soft gel in the intestinal tract. Because of its bland, inert nature, it may be used as a binder in compressed tablets. Since it is uniform in its thickening action, it is more efficient as a thickener than tragacanth, which is a variable mixture of bassorin, pectin and starch; or acacia which is composed

which is composed of arabic acid, arabin, gummic acid, bassorin, cerasin, dextrose and pentosan. It has been used in a wide variety of gum-less lotions, face and hand creams, leg make-ups and toothpastes. A typical formula for a dentifrice employing methyl cellulose is:

Methyl cellulose (400 centipoises)	10.0
Calcium Carbonate	450.0
Sodium Lauryl sulphonate	30.0
Alkyl - p - hydroxy-benzoate (preservative)	1.0
Flavouring oils	9.0
Glycerin	50.0
Water	450.0

Used in soap, methyl cellulose increases the hardness and improves the lather. A great potential use for methyl cellulose exists in preparations for use in opthalmology. Since a solution of methyl cellulose has a refractive index practically that of the cornea, it may be used with contact lenses. A solution of 1% methyl cellulose is useful for this purpose, as well as for a lubricant (artificial tears) in conditions where the lachrymal glands do not function adequately.

The classical eye solution has always been a simple aqueous solution of therapeutic ingredients. These solutions, even though they may be isotonic with lachrymal fluid, invariably cause an immediate flow of tears when placed in the eye, which tends to wash out the solution from the corneal surface before it may perform its full therapeutic action. The addition of methyl cellulose in approximately 0.5% concentration causes greater adherence to the active ingredients to be exerted on the condition being treated.

PREPARATION OF A SOLUTION OF METHYL CELLULOSE

There are two practical methods of preparing a solution:

1. Mix the methyl cellulose with approximately 30% of the water and allow to soak for half an hour. Add the remainder of the water as COLD WATER OR ICE. Bring to room temperature and stir until smooth.
2. Possibly a better method of preparing a solution is to wet the fibres with hot (nearly boiling) water, using 30% of the total water required. Then chill the resultant mass and add the remainder of the water as COLD WATER OR ICE.

The usual practice of adding all the water to the dry ingredient as in making solutions of most substances must be avoided, since water at room temperature will not completely dissolve the methyl cellulose, and the precipitate in the solution will consist of needle-sharp crystals which are irritating, especially in eye solutions. Wetting agents may be employed to hasten the manufacture of a solution, and will increase the viscosity.

When methyl cellulose is used as a thickening agent with insoluble substances such as zinc oxide, talc, and calamine, the dry ingredient may all be mixed together, and the liquid added in a mortar. Exact proportions of methyl cellulose to be used in such mixtures may be determined by experimentation.

REFERENCES

1. The New Methocel - Powdered Dow Methyl Cellulose, Published by the Dow Chemical Company, Midland, Michigan.
2. The Merck Index - Sixth Edition

Harry A. Smythe, Phm.B.
Hamilton, Ontario.

(Editor's Note - This article is the first submitted by a practising pharmacist to the Bulletin. We congratulate Mr. Smythe and invite others to submit manuscripts.)

The role of trypsin in the digestion of proteins in the intestinal tract has been well understood for many years. This enzyme is secreted in the pancreatic juice along with the fat-splitting enzyme steapsin, the starch-splitting enzyme amylase. Since they are present in the pancreatic juice, secreted by the pancreas into the intestine, they are often referred to as pancreatic amylase, pancreatic lipase (steapsin) and pancreatic protease (trypsin). The commercially available purified trypsin obtained from the glands of animals and thus is a by-product of the meat-packing industry.

All protein splitting enzymes, trypsin, pepsin and pancreatin have the ability to break down or digest protein. Since the body cells are made up of large protein molecules as structural units, it might appear that these ensymes would also break down the body cells. This ability to digest or break down tissue cells to the simpler and more easily assimilated amino acids is restricted to dead tissue cells.only. It can be readily understood that this happens in the body where the protein derived from dead tissue cells of animals is utilized by the body but the living tissue cells of the stomach and intestine are not affected.

This specific digestive power of trypsin and other proteolytic enzymes has been utilized in recent years to dissolve dead tissue in wounds and body cavities. It has been found that by digesting the dead tissue in wound areas and lung cavities with trypsin that normal tissue develops more quickly resulting in a more satisfactory healing of the injured or infected area.

Another use of trypsin has been revealed recently at the annual clinical congress of the American Congress of Surgeons. A purified trypsin is injected into the bloodstream and will then dissolve blood clots which have formed and have been deposited in the arteries and viens. The ability of trypsin to dissolve the blood clots should be of great value in the field of surgery. The antocoagulants such as heparin have only the ability to prevent the formation of the blood clot and can exert no dissolving action on the blood clot after it has been formed. Thus trypsin may prove as a useful adjunct in combating this surgical hazard.

The purified trypsin has been made available under the trade name ENZAR by Armour and Company.

R. M. Baxter

NALLINE - A NARCOTIC ANTAGONIST.

A new and specific narcotic antagonist is NALLINE, a product of Merck & Co. It represents antidotal treatment for overdosage of morphine and its derivatives and for Meperidine (Demerol) and Methadon (Amidone, Dolophine, Adanon). It is also recommended to combat the severe symptoms of extreme narcosis. The drug is not active against depression produced by barbiturates, cyclopropane or ether.

NALLINE is very similar in chemical structure to morphine. The only difference is that morphine's N-methyl ($N-CH_3$) group is changes to a N-allyl ($N-CH_2-CH=CH_2$) structure. This slight change is apparently sufficient to permit NALLINE to antagonize the pharmacological activity of morphine. That it is also an antidote for other drugs of different type structures, seems to indicate its action is not merely one of chemical competition.

The two branches of medicine in which this new drug is most useful, are surgery and obstetrics where morphine and other analgesics are used extensively. It aids in establishing breathing in infants born of heavily sedated (with morphine) mothers.

It is also very useful in surgical procedures in relieving respiratory depression caused by certain narcotics.

NALLINE has little or no analgesic effect itself but since it is a derivative of morphine, it is subject to the regulations of the Opium and Narcotic Act. An emergency drug of this sort should be stocked in all dispensaries.

G. R. Paterson

REGISTRAR'S OFFICE.

In the May number of the Bulletin I told you something of the amendment to the Pharmacy Act passed at the last session of the Legislature dealing with Fees. A number of the pharmacists wrote to me asking what the fees would be, but as Council had not passed the necessary By-laws required by the Act, I could not give the information desired.

The By-laws have now been approved, and a letter giving all details is being mailed to you. However, in order that you may have them in brief form, I am listing here the fees payable.

You will note that there has been no change in the fees to be paid by individual owners, managers of stores, or dispensaries, assistant managers, partnerships, or estates. The only fee that is higher is that of Directors, who pay both the fees as director and as member of the College. Where a Director is also Manager he pays the Manager's fee as well.

All Members of the College (except those listed below)	$10
Independently owned pharmacy	
Owner	15.
Each Branch pharmacy	15.
Each branch manager	15.
Simple Partnership	
Each partner	15.
Estate	15
Manager of Estate	15.
Incorporated Company.	
Each Director (in addition to the $10 Membership Fee)	15.
Manager	15.
Each branch	15.
Pharmacists in Hospitals	
Chief Pharmacist	15.

Fees are due on January 10, 1953.

H. M. Corbett
Registrar-Treasurer

A committee of 6 medical experts has reported that the controversial drug, Krebiozen, is ineffective in the treatment of cancer. Announcement of the drug's reported potentialities for treatment of cancer attracted attention last year. The product was developed by a Yugoslav refugee, who refused to disclose his secret formula. - American Druggist, September 29, 1952.

RECENT RESEARCH IN HYPERTENSION

Hypertension (high blood pressure) has many and varied causes. The symptoms of certain types can be controlled by the use of certain specific drugs and in other cases, surgery. One form of hypertension is associated with an increased amount of epinephrine and nor-epinephrine in the blood stream. These hormones, which in normal patients are secreted by the adrenal cortex, will cause high blood pressure if present in too large amounts in the blood stream. Research workers found that certain hypertensive patients have tumors of the adrenal glands. These secrete epinephrine and nor-epinephrine as does the adrenal gland. Thus if these tumors are removed by surgery the hypertension may be reduced. However, before surgery an accurate diagnosis is necessary. A new drug Phentolamine (Ciba) (also known as Regitine) has been found to block the action of epinephrine and nor-epinephrine thus resulting in a drop in blood pressure. Thus the drug may be used as a diagnostic agent as well as an agent for the temporary relief of the symptoms. This new compound has not as yet been generally released but is still being evaluated.

R. M. Baxter

CUMULATIVE INDEX

	page
An Appeal from the Dean's Office	7
Buying	11
Chloromycetin	25
Chlorophyll Ointment and Suppositories	6
Compenamine, A New Penicillin Salt	12
Cost of Operating Pharmacies in Ontario in 1951	20
Dean's Office	1
Drug Fatalities	12
Extension Lectures	11, 19, 25
Food and Drug Act Changes	11
For Women Only	13
Glycerin Substitutes	13
Glycerin-Sulphonamide Paste for Burns	12
History of Pharmacy in Ontario	4
Hypospray for Jet Hypodermic Injection	12
Isonicotinic Acid Hydrazide in Tuberculosis	28
Isopropyl Alcohol in Pharmacy	14
Library	6
Memorial Library	10
Methonium Compounds	26
Methyl Cellulose	29
Nalline - A Narcotic Antagonist	31
New Penicillin Compound.	8
New Uses for the Enzyme, Trypsin	31
Next Natural Step for the Ontario College of Pharmacy	17
Organic Chemistry and the Pharmacist	14, 5
3-ortho-toloxyl-1, 2-propanediol	27
Pharmaceutical Problems	9, 16
Plant and Animal Products in Pharmacy To-day	5, 10
Prescription Surveys	12
Problems of European Prescriptions	9
P - 92 Penicillin	13
Recent Research in Hypertension	33
Registrar's Office	1, 8, 27, 32
Selenium Disulphide	14
Sorbitan Derivative in Pharmacy	2
Statement of Purpose	1
Story of the Books	10
What is Tar Ointment ?	13
Where You Can Get Them - Sources and Prices	17

BLACK VOICE